

**REMARKS**

Applicants request reconsideration of the above-identified application in view of the foregoing amendments and following remarks.

Applicants have amended claim 34 to recite a PAMP "function-conservative variant" and the specific functions associated with such variants. Support for these amendments can be found on, for example, page 15, lines 4-31; page 25, lines 11-24; and in Examples 1 and 2.

Applicants have amended claim 35 to recite an "isolated" mutant PAMP, to delete the recitation of mutant PAMP fragments and substantially homologous mutant PAMP fragments, and to recite the limitation that the claimed PAMP mutant is at least 80% identical or 90% similar to the corresponding native protein. Support for these amendments can be found, for example, on page 15, lines 4-31.

Applicants have amended claim 36 to depend from claim 35, to recite an "isolated" mutant PAMP, to delete the recitation of mutant PAMP fragments, and to recite specific biochemical changes associated with PAMP mutations. Support for these amendments can be found in, for example, Examples 1 and 2.

Applicants have amended claim 37 to improve its form, to recite an "isolated" mutant human PAMP, and to delete the recitation of mutant PAMP fragments.

None of the new claims presents new matter.

Claims 34-37 remain pending in this application.

### **Maintained Rejections**

#### **35 U.S.C. § 112, Second Paragraph: Indefiniteness**

Claims 34-36 are rejected under 35 U.S.C. 112, second paragraph, for allegedly being indefinite. Each part of the rejection is discussed separately below.

The Examiner states that, in claim 34, no function is assigned to the recited "function conservative fragment" of PAMP. The Examiner states that, while applicants have urged that one skilled in the art would understand such a fragment in light of the specification, the intended function of the fragment is not set forth in the claim. The Examiner further states that "[i]n order for one to determine which fragment of PAMP is intended, an assayable function must be attributed to the fragment."

Applicants traverse. In light of the teachings of the specification, one of ordinary skill in the art would recognize and understand that a function-conservative variant refers to any PAMP variant which retains a function attributed to full-length PAMP. However, solely to expedite prosecution, applicants have amended claim 34 to recite specific PAMP functions associated with the claimed function-conservative variants of PAMP.

With regard to claim 36, the Examiner argues that the biochemical changes similar to those associated with mutations in presenilin-1, presenilin-2 or  $\beta$ -amyloid precursor protein are unclear.

Applicants traverse. In light of the specification, the skilled worker would understand and recognize the metes and bounds of the phrase "biochemical changes similar to those associated with mutations in presenilin-1, presenilin-2 or  $\beta$ -amyloid precursor protein". However, solely to expedite prosecution, applicants have amended claim 36 to recite specific biochemical changes in  $A\beta_{42}$  peptide levels,  $A\beta_{40}$  peptide levels, or  $A\beta_{42}/A\beta_{40}$  peptide ratio.

In the context of claim 35, the Examiner argues that a mutant PAMP substantially homologous to human, mouse or *D. melanogaster* PAMP is not clear. According to the Examiner, it is unclear as to whether man-made mutations in human, mouse or *D. melanogaster* PAMP would be considered substantially homologous or if other species of PAMP would be considered mutant PAMPs. The Examiner additionally states that the term "substantially homologous" is indefinite because it is unclear which regions are homologous.

Applicants traverse. Solely to expedite prosecution, however, they have amended claim 35 to delete the recitation of substantially homologous mutant PAMP fragments and to, instead, recite the limitation that the claimed PAMP mutant is at least 80% identical or 90% similar to the corresponding native PAMP protein. One of skill in the art would be able to, simply and without undue experimentation, determine the % identity and % similarity of a protein, with respect to PAMP, using a variety of well known programs and methods (see, for example, page 15, lines 4-21). Accordingly, the metes and bounds of amended claim 35 would be clear to the skilled artisan.

In light of the above arguments and amendments, applicants respectfully request that the Examiner reconsider and withdraw the 35 U.S.C. § 112, second paragraph, rejections.

35 U.S.C. § 102(a)

Claims 35 and 36 stand rejected under 35 U.S.C. 102(a) as allegedly being anticipated by the *C. elegans* Sequencing Consortium ("Consortium"). According to the Examiner, the Consortium teaches an amino acid sequence that shares 99.7% identity to *C. elegans* PAMP (SEQ ID NO: 12) and the instant specification teaches that this homologue is identical to the sequence disclosed by the Consortium. The Examiner states that claims 35 and 36 are anticipated by the Consortium reference "because one PAMP can be considered to be a mutant of the PAMP of another species; thus, the *C. elegans* PAMP is a mutant of the human, mouse, and *Drosophila* PAMP". The Examiner further states that *C. elegans* PAMP is substantially homologous to human, mouse, or *D. melanogaster* PAMP and that it is considered to comprise a functional fragment of the human, mouse, and *Drosophila* PAMP. Applicants traverse.

However, solely to expedite prosecution, applicants have amended claim 35 to recite the limitation that the claimed PAMP mutant is at least 80% identical or 90% similar to the corresponding native PAMP protein. The specification teaches that the human PAMP protein has 22% sequence identity and 39% sequence similarity to the *C. elegans* protein (see Example 1, particularly page 32, lines 15-21). In addition, applicants demonstrated, in their August 15, 2007 Response, that mouse PAMP has 21% identity and 41% similarity to *C. elegans* PAMP while *D. melanogaster* PAMP has 23% identity and 41% similarity to *C. elegans* PAMP. Because *C. elegans* PAMP does not satisfy the limitations of amended claim 35, the Consortium sequence does not anticipate claim 35 (and dependent claim 36).

In light of the amendments and arguments presented above, applicants request that the Examiner reconsider and withdraw the 35 U.S.C. § 102(a) rejection of the pending claims.

### **New Objections and Rejections**

#### **The Objection**

The Examiner objects to claim 36 for depending from non-existent Claim 39.

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Applicants have amended claim 36 to depend from claim 35 thus obviating the objection.

35 U.S.C. § 101

Claims 35 and 36 stand rejected under 35 U.S.C. § 101 for allegedly being drawn to non-statutory subject matter because the claimed proteins are not stated to be isolated or purified.

Applicants have amended claim 35 (and thus dependent claim 36) to recite an "isolated" PAMP thus obviating the Examiner's rejection. Because claim 36 depends from claim 35, its rejection is also obviated.

35 U.S.C. § 102(b)

Claims 35-37 stand rejected under 35 U.S.C. § 102(b) as being anticipated by a single amino acid such as alanine. According to the Examiner, because claims 35 and 37 are drawn to a fragment of mutant PAMP without an assigned activity, alanine would qualify as such a fragment.

Applicants have deleted the recitation of mutant PAMP fragments from claims 35-37 thus obviating the Examiner's rejection.

35 U.S.C. § 112, First Paragraph: Written Description

The Examiner has rejected claims 35-37 for allegedly failing to comply with the written description requirement. The Examiner states that because the claims do not correlate the mutant PAMP fragments with a defined activity, applicants are not in possession of the fragments. Applicants traverse.

However, solely to expedite prosecution, applicants have deleted the recitation of mutant PAMP fragments from claims 35-37. Thus the Examiner's rejection is obviated.

The Examiner has rejected claim 34 for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to the skilled artisan that the applicants were in possession of the invention at the time of filing. The Examiner states that the term "functional conservative fragments" of PAMP is not taught in the specification. The Examiner notes, however, that



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"functional-conservative variants" are defined on page 15,  
paragraph 2, of the specification.

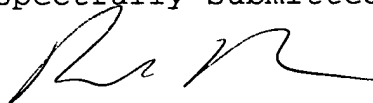
Applicants have amended claim 34 to recite "function-  
conservative variant" thus obviating the Examiner's rejection.

In light of the amendments and arguments presented  
above, applicants request that the Examiner reconsider and  
withdraw the new rejections of the pending claims.

#### Conclusion

Applicants request favorable consideration of the  
application and early allowance of the pending claims.

Respectfully submitted,



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James F. Haley, Jr. (Reg. No. 27,794)  
Attorney for Applicants  
Raymond M. Doss (Reg. No. 61,000)  
Agent for Applicants  
ROPES & GRAY LLP  
Customer No. 1473  
1211 Avenue of the Americas  
New York, New York 10036  
Tel.: (212) 596-9000  
Fax: (212) 596-9090